ANGIO-NEUROTIC OEDEMA AND THE ANGIO-NEUROSES.

M.D. 1911

Thesis submitted for the M.D. Edinburgh

by

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ANGIO-NEUROTIC OEDEMA AND THE ANGIO-NEUROSES.

Introduction.

A number of conditions may be included under the term Angio-Neuroses——localised oedema, urticaria, erythema, Henoch's Purpura, erythromelalgia, Raynaud's disease, scleroderma and probably bronchial asthma and hay fever. All are characterised by a marked disturbance of the vascular tonus in addition to a more or less pronounced inflammatory condition of the skin and mucous membranes. They may be divided into two groups of disorders, the one in which a contraction of the vessels takes place, as in Raynaud's disease, the other in which localised vascular dilatation or exudation (serous or haemorrhagic) is the prominent feature.

Most observers consider them all to be caused by some functional disturbance of the sympathetic nervous system due in many cases to an obvious toxaemia, or sometimes to some unknown irritant occurring in a neuropathic individual, several of the conditions alternating in the same patient at different times.

Osler in 1888 (New York Med. Jour. 1888) advanced the theory that the entire group may depend on some poison which in varying doses and in different constitutions excites in one urticaria, in a second peliosis rheumatica and in a third a fatal form of purpura.

In Henoch's Purpura the view is widely accepted that the abdominal colic is due to an angio-neurotic oedema of the intestine.

Colin Campbell recorded a case of angio-neurotic oedema, urticaria and asthma in a lady aged 26 at the Liverpool Medical Institute (B.M.J. Mar. 5th, 1910, p.573).

Other writers have recorded cases of asthma and urticaria alternating in the same individual.

Under the nomenclature of angio-neurotic oedema, giant urticaria, wandering oedema, and acute recurrent oedema, observers are fairly unanimous in describing a group of symptoms consisting of an abnormal tendency of the skin and mucous membranes to react to slight and varied irritants with the production of inflammatory changes (dilatation of the vessels and exudation) usually transitory in nature and which may be regarded as constituting a distinct disease.

Milton reported cases as giant urticaria in 1876 (Edinburgh Med. Journal 1876), but general attention was more particularly drawn to this condition by Quincke in 1882 (Monatsheft f. prakt Dermatologie 1882) and it is sometimès referred to as Quincke's Oedema.

In 1892 Banke drew attention to a "circumscribed oedema" which sometimes occurred suddenly in patients with some neuropathic tendency in which the oedema was painless and subsided after a day or so, leaving no bad results.

Although many writers describe bronchial asthma, hay fever, and acute pulmonary oedema as distinct diseases in the light of our present knowledge, it would be perhaps better to include them as symptoms of angio-neurotic oedema, with which disease they are so often associated and with which at any rate they are intimately connected.

Theo Diller has reported two interesting cases of angio-neurotic oedema (New York Med. Jour. Mar. 3rd, 1906) in neuropathic women, which supports this view.

One patient a married woman of 51, had been the subject successively of attacks of (1) spasmodic asthma beginning with "cold in the head" from the age of 32 to the age of 44, (2) spasmodic headache from the age of 44 onwards; and (3) angio-neurotic oedema from the age of 48 onwards; the attacks of oedema alternating with the headaches.

The other patient a woman of 26 became subject to acute circumscribed oedema affecting various parts of the body, and which later were associated with attacks of vivid hallucinations of sight and hearing with accompanying feelings of horror.

Erythema and urticaria are by many observers considered to be but milder manifestations of the same disorder.

In the present thesis the writer has attempted to give an exposition of the present day views on the whole subject and to give an account of some cases under her own observation.

Etiology.

There is still much obscurity as to the cause of this disease but most observers are agreed that it is due to a toxaemia occurring in a neuropathic individual. In almost all the recorded cases, one and usually both of these factors have been present in varying degree.

Ernest Wills and Dudley Cowper reported five cases of "circumscribed oedema" (Journal of Neurology 1903). In every case there was some marked neuropathic lesion, while all the patients were free from any organic disease which could have had any influence at all on the production of this condition.

The temperature was not raised, the oedema was painless, and the general health was undisturbed. The authors therefore considered that hysteria, hystero-epilepsy, neurasthenia and such-like emotional conditions should be recognised as among the chief predisposing causes, and that psychical disturbances should be placed first among the exciting causes, and in this opinion they recorded the opinion of Banke, Charcot and others.

Louman (in B.M.J. April 14th, 1906) records two cases, one in which the eyelids were involved and the attack was brought on by fright, and which was relieved by the administration of potassium bromide, and the second in a nervous man of 55 in whom worry would bring on an attack.

In Fèrés Pathologie des Emotions (chap. VI.) there is an account of various skin diseases that have been produced apparently by painful emotions, namely local syncope, erythema, urticaria, purpura, eczema, psoriasis, herpes, pemphigus, prurigo and vaso-motor oedema, all of which may be properly classed as angio-neuroses.

With regard to herpes labialis I have seen so many cases occurring in young neurotic women as a sequelae to some emotion, sometimes pleasurable as when due to the anticipation of a dance or other social festivity, but more frequently due to some anxiety or worry, that I always regard this condition especially as of vaso-motor origin, the frequency and severity of the attacks often lessening as the nervous system becomes more stable.

Insanity curiously enough does not seem to predispose to the disease and in the writers own experience of two years of asylum work she does not recollect seeing a single case, the cases recorded which are associated with mental symptoms being acute and of such short duration and rarely requiring asylum treatment, the insanity being the effect rather than the cause of the condition.

Heredity plays an important part in some cases and Osler records a very interesting case in which several members of a family were affected in different generations. (Practice of Medicine, Osler and Macrae,

Vol. 6. p.648). In the same contribution he gives as other exciting causes, the infectious diseases, various psychoses, the climacteric, menstrual disturbances, alcohol and morphine.

Max Joseph records three cases occurring in dipsomaniacs and gives as exciting causes the climacteric, onset of puberty, exhaustive nervous drain, masturbation and gastric irritation.

In one of my own cases menstrual disturbances seemed to be responsible for the condition.

Toxaemia often produces an attack. Lemaire in (L'Echo Med. du Nord. May 27th, 1906) holds the opinion that the toxins may be digestive or specific e.g. rheumatism,and produce the disease in patients of a neuro-arthritic temperament. He records the case of an acute attack in a man of 29 who had symptoms of gastric and hepatic catarrh, articular pains in shoulders and knees, followed by painless oedema of eyelids. The administration of aspirin gave relief.

The association of urticaria with the ingestion of poisonous substances is well known, and though the cases are more acute and in many cases respond more readily to treatment, the difference is one of degree only.

Carious teeth, boils, or other small septic foci, have sometimes proved to be the exciting cause of an attack and Capt. C. R. Sylvester Bradley records two

cases. (Jour. R. Army Medical Corps July 1910) of typical angio-neurotic oedema occurring in soldiers of which the only exciting cause appeared to be carious teeth and in which it was difficult to find any neuropathic tendency.

Sex seems to be unimportant though probably women owing to their more excitable nervous systems suffer more than men.

Age seems to limit the disease somewhat as it is rarely seen in children or the aged and occurs most frequently in young adults.

Pathology.

To understand the pathology of this condition it will be necessary to refer briefly to the anatomy and physiology of the sympathetic nervous system.

It is now recognised that the sympathetic nervous system is not an independent system but is intimately connected with the brain and spinal cord.

The vascular tonus is therefore controlled by a complex nervous mechanism, consisting not only of the vaso-constrictor and vaso-dilator nerves, which are connected with the larger sympathetic ganglia, but also with centres in the spinal cord connected with the higher centres in the brain.

The brain centres in turn are complex consisting of an automatic mechanism in the medulla regulating the action of the subordinate parts below it, and of a series of cortical centres whose function it is to stimulate or inhibit the medullary mechanism.

It is therefore evident that the vascular tonus may be modified not only by local causes acting on the ganglia in the walls of the arterioles, but also by changes in the sympathetic ganglia as seen in the hyperaemia of the face produced by lesions of cervical ganglia, by reflex action through the spinal cord as seen in the pallor produced by pain, or indirectly by impulses from the cortex as in the blush of shame.

Wills and Cowper (Brain 1893) ascribed the pathology of the condition to a local paralysis of the vaso-constrictors or a reflex stimulation of the vaso-dilators, resulting in a retardation and stasis of the blood. An exudation from the capillaries then follows, usually serous but sometimes sanguineous.

The special characteristics of the disease as compared with the other angio-neuroses, are its fleeting nature and the almost bizarre distribution of its symptoms, and thus most observers consider it due to a purely functional condition without any gross pathological change. It is difficult to understand why the oedema flits from place to place and as yet no satisfactory explanation is forthcoming.

Recently a good deal of evidence has been brought forward to show that there is a deficiency of lime salts in the blood in these conditions and at the last meeting of the British Medical Association July 1910, there was a most interesting discussion on vaso-motor rhinitis (localised angio-neurotic oedema) and several of those who took part in the discussion testified to the value of the administration of calcium salts in this condition. Mr. E. B. Waggett concluded "that this was sufficient to prove that the phenomena are associated with blood chemistry just as the local oedema of skin urticaria is dependent on the saline contents of the blood" (referring to the work of Professor Wright on this subject.).

Dr. Watson Williams also stated that he believed that a certain proportion of the cases under discussion were due to bio-chemical changes in the blood, affecting the bulbar centres.

At the same meeting Professor Hans Meyer read a paper on the action of lime salts, on experimental work that had been done in his own laboratory, and he is of the opinion that it has been demonstrated that the administration of lime salts diminishes the permeability of the walls of the blood vessels, hence it is conceivable that a deficiency of these salts increases the permeability of the walls under certain conditions.

While considering the evidence in favour of this theory of calcium deficiency in these cases it is interesting to refer to a case of Henoch's Purpura (abdominal angio-meurotic oedema) recorded by Stewart Macmillan in the B.M.J. Nov. 26, 1910, in which after several drugs had been tried in vain, complete recovery followed the administration of calcium lactate.

At present it is impossible to state with any certainty what the pathology of this condition is, as our knowledge of the subject is very imperfect, but there are indications that show that a more intimate knowledge of the chemical changes in the blood in these conditions would prove of infinite value, and would form a radical basis for treatment.

Symptomatology.

Cases.

CASE 1. Hospital Probationer. A.B. aged 22, was an apparently strong, healthy, intelligent girl, who had been nursing for three months only and had suffered from amenorrhoea during that time. Her previous health had been good and menstruation regular. She complained of a rash over both hands and a "stiff face" but otherwise felt well. The amenorrhoea had not troubled her and she did not suffer from constipation.

On examination she was found to have well-marked nettle-rash over the dorsum of both hands spreading up above the wrists. Though there was considerable erythema she did not complain of much irritation. The face was considerably swollen especially the upper part and the loose tissue about the eyes suggesting at first sight a case of acute nephritis. There was no pain or tenderness and no local cause such as a decayed tooth, inflamed tonsils or scratch could be found; the temperature was 99°F and the pulse 80. There was slight cutaneous oedema over the chest and well marked dermographia.

Heart and lungs were normal. The urine had a Sp. Gr. 1020 and contained no sugar nor albumin, but had a fairly heavy deposit of oxalates.

The tongue was clean and there was apparently no gastro-intestinal torpor.

It was evidently a case of angio-neurotic oedema and some anxiety was felt lest oedema of the glottis should occur. The amenorrhoea was probably the cause of the condition. A hot hip bath was ordered night and morning and a hot rubber bottle was applied constantly to the abdomen. A draught composed of mag. sulph. and mag. carb. was given before breakfast, and a diet of fish and milk prescribed. The oedema of the face increased towards night-time but was fairly symmetrical. The next morning however it was considerably less and the day following that menstruation reappeared and the oedema of face and urticaria of hands rapidly disappeared.

There was nothing of interest in the family history so far as could be obtained and the girl was not obviously neurotic, and the attack must be explained by some toxaemia due to the amenorrhoea acting on a somewhat unstable vaso-motor apparatus.

Though the symptoms were mild it is an interesting case as showing the association of angio-neurotic oedema, urticaria and dermographia in the one patient all occurring at the same time.

CASE 2. J.C. aet. 22, was a pale anaemic man who had been in hospital for 3 years, and who was under the writer's observation for a year. He was known to suffer from haemophilia and there was a history of severe bleeding after a cut when a child and also after

the extraction of a tooth while in hospital. He suffered from arthritis of various joints which at one time was thought to be rheumatic because it appeared to be relieved by sod. sal., and yet at times suggested a tubercular origin. The arthritis however was peculiar in some respects, it affected several joints altogether but rarely more than one at a time, thus both knees, both elbows, left wrist and left hip were affected, the right knee and left elbow being once affected together. The joint would be slightly red, tender and swollen, and the temperature would rise to 99° or 100°F the pulse being about 90. The swelling would subside in a week or two and the patient allowed up till another joint was attacked. An exploring needle was inserted into one knee during an attack.and unaltered blood withdrawn and although there was no history of injury before the attack and no bruising on ecchymoses to be seen, the case was then considered to be one of haemophilia.

The swelling of the joint subsided after some weeks and no thickening or contracture was left.

Treatment was unsatisfactory. Sod. sal. certainly relieved the pain, but prolonged treatment with bipalatinoids of arsenic iron and strychnine appeared to suit him best. Cod liver oil and calcium chloride were tried but were of little use. The local treatment consisted of painting with diluted liniment of iodine and this certainly seemed to be efficacious in limiting the arthritis to a certain degree.

Garrod (Quart. Jour. Med., Oxford 1910, III.208) has formulated the notion of articular erythemas and it is reasonable to suppose that these may develop into serous or even haemorrhagic exudations in the synovial membranes. The case cited above had certainly several features peculiar to angio-neurotic oedema and the writer feels justified in recording it as such, the fleeting nature of the arthritis, slight constitutional disturbance and response to tonic treatment all supporting this view.

The family history in this case was negative but the patient himself was of slightly neurotic temperament, and was probably suffering from some obscure toxaemia.

In the two cases recorded above some of the manifestations of angio-neurotic oedema are well illustrated, but they may be many and varied and should include those commonly seen in the allied conditions—asthma, hay fever, Henoch's Purpura and similar affections. It will be simpler therefore to describe them under the affected system.

In most cases they are of more or less limited extent and of transient duration.

Cutaneous System.

Some of the more common symptoms arewell seen in Case 1, When marked the oedema is often circumscribed and may affect the lips, arms or legs and often flits from place to place. The eyelids are often affected and the writer saw one case in a girl of ten, who had been playing

in the snow, both eyelids were affected, but the oedema had quite disappeared the next morning; this patient was also subject to chilblains.

In another neurotic female patient aged 52, the underlip would suddenly swell, usually after some emotional disturbance, the condition persisting for a few hours and then disappearing.

Herpes labialis is another common cutaneous symptom and may be the only one.

Alimentary System.

The tongue is sometimes swollen and oedematous and frequently the oedema affects the epiglottis and is often fatal. In Henoch's Purpura the mucous membrane of the bowel is affected causing intense abdominal pain, sometimes accompanied by melaena and often associated with cutaneous oedema and purpura. The attacks are usually acute and the symptoms subside suddenly, often when the patient has appeared to be in extremis.

Pulmonary System.

In vaso-motor rhinitis the mucous membrane of the nose is affected, and there is also a watery discharge, this condition is more localised and is often associated with urticaria. Although due in most cases to a specific irritant, such as pollen, and periodic in character, the attacks are similar and closely allied if not identical with those of angio-neurotic oedema.

In bronchial asthma we have another local manifestation and Colin Campbell exhibited the case of a lady at the Liverpool Medical Institute who suffered from angio-neurotic oedema, urticaria and asthma (B.M.J. March 25th, 1910, p.573).

Cases of acute pulmonary oedema are probably but symptoms of a similar condition, the sudden onset and short duration negativing any organic disease. Coplin (Ther. gaz. April 1906) suggested a toxic cause for these attacks, and others have also attributed them to vaso-motor disturbance in the lungs.

Circulatory System.

The causes of so-called pseudo-angina-pectoris occurring in neurotic women without organic disease and often relieved by applications of heat to the extremities have also been ascribed to vaso-motor changes.

Dr. Francis Hare in a letter to the Lancet (Sep. 30th, 1905, p.991) on "Angina Pectoris and Allied Conditions" makes some very interesting statements and suggestions as to the cause of the pain in this condition. He brings forward the hypothesis that the pain of angina depends upon vascular distension in the mediastinum. The vascular distension would depend upon vaso-dilation in these areas, and the vaso-dilation would be compensatory of the well-known vaso-constriction in the peripheral circulation, which is one of the most constant phenomena

of angina pectoris. He continues "Frequent vaso-dilation would on Thoma's view explain the common occurrence of arterio-sclerosis of the coronary arteries just as the long recurrence of the same vascular condition explains the arterio-sclerosis of the temporal artery in cases of old-standing migraine". "The view here enunciated is consistent with the vaso-motor view of the mechanism of migraine and asthma, affections connected by the closest ties with the 'functional' form of angina-pectoris".

Nervous System.

The symptoms of migraine and epilepsy could both be explained if regarded but as those of localised cerebral angio-neurotic oedema. Reference has already been made to Dr. Francis Hare's opinion as to the intimate relationship of migraine, asthma and pseudo-angina pectoris, and there is a growing tendency to include epilepsy in the same category. Certainly the neuropathic inheritance and the often transient and periodic nature of the attacks which are so frequently associated with some apparent toxaemia or strong emotion, give some justification for this view.

Genito-Urinary System.

Certain so-called hysterical cases of anuria are very suggestive of vaso-motor disturbance and might doubtless well be classed as one of a general affection of the sympathetic nervous system.

The symptoms associated with many cases of dysmenorrhoea and those occurring during the climacteric are probably often due to a general vascular disturbance as shown by the quickened pulse, flushings and nervous symptoms.

Locomotor System.

Case II recorded above is a good example of the probable affection of the joints in this condition and as further support to this diagnosis, Dulche in an article on "Puberty in the Female" (Jour. de prat Sep. 17th, 1910) states that among other vaso-motor symptoms, hydrarthrosis and a condition similar to "Potts disease" or "white swelling" is sometimes seen.

Another interesting case of angio-neurotic oedema with one elbow joint affected, associated with oedema of the face and eyelids has also been recorded by a writer in the International Clinics (Vol. IV. Page 112). The patient was a debilitated neurotic woman, and the temperature remained normal throughout the attack, which soon subsided under palliative treatment. Reference has already been made to Garrod's views on articular erythemas.

It will be seen therefore that the symptoms are not confined to the cutaneous system as was formerly supposed but may affect almost any organ in the body, their onset, course and duration being very similar

in all cases, and characterised usually by some nervous disturbance, the symptoms often alternating in one patient, and a marked neuropathic heredity being nearly always present.

Such being the case the writer is of opinion that as the pathology of them is probably identical it is more convenient to class all the symptoms under the head of angio-neurotic oedema.

Treatment.

The treatment of angio-neurotic oedema is often difficult and unsatisfactory and is chiefly symptomatic, though the general condition of the patient must always be considered. The nervous element must never be lost sight of, nor any peripheral irritation or general toxaemia.

In most cases it is better to keep the patient in bed on a milk or light diet according to the severity of the symptoms.

Warmth in the form of hot water bottles applied to the feet, spine and abdomen often gives relief, and a dose of calomel followed by a saline is often indicated, though the writer prefers to omit the calomel as she has seen cases of acute erythema follow its use in susceptible people.

There is no drug known which has an unfailing beneficial effect on this condition, but a few have been tried with success when there have been definite indications for their use, but in spite of all treatment the attacks tend to recur, often periodically.

Morphia is often useful in asthma and angina but it has the drawback that the morphia habit is encouraged.

Belladonna and atropine should always be tried when the mucous membranes are affected. Dr. L. Gwilliam

Davies (B.M.J. July 30th, 1910) has recorded a most interesting case of acute pulmonary oedema in which the symptoms were most urgent and which responded well to large hypodermic injections of belladonna tincture and the patient made a good recovery. It is probable that this treatment tried early might be equally effective in those cases where the oedema has affected the epiglottis and which so often prove fatal.

Potassium bromide sometimes gives relief if there is any marked emotional condition present as in Lonman's case referred to previously. Its use in epilepsy is of course well known.

Sodium salicylate or aspirin have been given with benefit as in Lemaires case, when there has been evidence of a rheumatic condition.

Adrenalin and arsenic are sometimes useful where there is a haemorrhagic exudation. Longley has recorded a case (B.M.J. 1906) of Henoch's Purpura in a girl of eleven where these drugs acted like a charm. The girl had suffered from various tubercular joint lesions and developed a rash chiefly on her legs ten days after a soaking. It was accompanied by joint pains and a slight temperature and two days afterwards she felt much better. Four days later vomiting and abdominal pain set in, the child evidently collapsing. Morphia suppoditories gave some relief and she was able to take milk and soda and was given bismuth and chlorodyne.

The condition persisted on and off for three weeks the abdominal symptoms being worse when the skin rash abated. At the end of this time a more severe attack complicated with haematuria occurred. Morphia suppositories gave no relief. Adrenalin min 2 and liquor arsenicalis min 3 were given four hourly with rapid alleviation of the symptoms.

Iron either alone or in combination with arsenic and strychnine has sometimes been found useful when anaemia was present as in Case II above recorded by the writer.

The calcium salts are indicated if the coagulability of the blood is diminished and have been used successfully in chilblains, hay-fever, urticaria and Henoch's Purpura. Erasmus Paramore (Brit. Journ. Derm. July and Aug. 1906) gives an account of some research work in cases of urticaria in which by the administration of a calcium salt he cured the condition. Milk does well in these cases because of its lime contents. Their use in vaso-motor rhinitis and similar conditions has already been referred to under the head of Pathology. Probably, their efficacy depends not only on the individual's power of absorption of these salts but also on the salt employed, the lactate apparently being the most useful in these conditions. Stewart Macmillan (B.M.J. Nov. 26th, 1910) has recorded a case of Henoch's Purpura which was successfully treated with calcium lactate.

Nasal cauterisation has proved extremely useful in some cases of asthma, hay-fever and other vaso-motor neuroses and at the B.M.A. meeting 1910, Dr. A. Francis read a paper on cases of his own successfully treated by this method. The rationale of the treatment is difficult to understand but it may be explained apparently either by some reflex action on the vaso-motor centres in the medulla, and in some cases by its influence in lessening arterial tension.

Tracheotomy must be resorted to in some cases of severe oedema glottidis.

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